REMARKS

I. Status of the Claims

Claim 19 has been amended. Claims 27 and 28 have been canceled. Claims 57 to 72 have been added. The amendments do not encompass new matter being supported generally throughout the specification, including at least page 10 to 11. Claims 19-21, 29-33, and 51-72 are pending.

II. Sequence Listing Requirements

Applicants have amended the specification to include identification of the oligonucleotide disclosed on page 33, line 5 of the specification by SEQ ID NO:17. The sequence listing has been amended to include the sequence of the oligonucleotide as SEQ ID NO:17. A supplemental sequence listing accompanies this response. Applicants respectfully request the withdrawal of the objection related to compliance with sequence disclosure.

III. Priority

The Action objects to granting claims 51-55 the benefit of priority to provisional application serial number 60/137,665 (the '665 application) filed on June 4, 1999. The Action alleges that the provisional patent application does not provide an adequate disclosure for SEQ ID NO:2 to support claims 51-55 as of June 4, 1999. Applicants respectfully traverse.

Claims 51-55 are directed to viral genomes comprising various contiguous nucleotides of SEQ ID NO:2. SEQ ID NO:2 is the full length, infectious GBV-B viral genome that includes the 3' GBV-B sequence, *i.e.*, the known 5' sequence and the newly identified 3' sequence. Description of SEQ ID NO:2 is provided at least on page 4 lines 6 through 25 of the '665 application that reads in part:

> The construction of an infectious molecular clone of this virus will require the newly determined 3' sequence to be included in order for the clone to be viable...This sequence has been reproducibly recovered from tamarin serum [] as a fusion with *previously reported 5' GBV-B sequences*. [] The newly identified 3' sequence is not included in *published reports of the GBV-B sequence, nor described in patents relating to the original identification of the viral sequence* (see U.S. Patent No. 5,807,670 and references therein). (emphasis added)

and page 9, lines 6 through 8 that reads:

> Nucleic acids according to the present invention may encode the 3' sequence of the GBV-B genome set forth in SEQ ID NO:1,[or] *the entire GBV-B genome*... (emphasis added).

Furthermore, on page 32 of the specification Applicants disclose Genbank accession number U22304 dated April 12, 1995 (Exhibit A). Genbank accession number U22304 contains a GBV-B genomic sequence representative of the published GBV-B sequence that lacks the 3' GBV-B sequence (SEQ ID NO:1). One of skill in the art had access to the nucleotide sequence disclosed in Genbank accession U22304, as disclosed in the provisional '665 application.

In regard to enablement, the standard for satisfying the enablement requirement under 35 U.S.C. §112 is provision of a description in the specification so one skilled in the art can practice the invention without resorting to undue or unreasonable experimentation. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). See also *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent *coupled with information known in the art* without undue experimentation.") (emphasis added). The '665 application enables one of skill to practice the invention of claims 51-55, particularly in light of information known in the art, *e.g.*, the previously cloned 5' portion of the GBV-B genome. Claims 51-55 are directed to methods of producing a GBV-B or GBV-B chimeric virus related to the nucleic acid sequence of SEQ ID NO:2, which is the full length

GBV-B sequence inclusive of SEQ ID NO:1. One of skill in the art would readily, in light of the disclosure of the provisional '665 application, be able to infect a host cell and produce an infectious GBV-B virus or Chimeric GBV-B virus as of June 4, 1999.

Furthermore, the written description provided above is also sufficient to convey to one of skill in the art that the Applicants' possessed the invention of claims 51-55. Based on the disclosure of the '665 application one of skill would be in possession of SEQ ID NO:2, which is the combined sequence of Genbank accession number U22304 and the 3' nucleotide sequence of GBV-B (SEQ ID NO:1) as described in the '665 application. The case law does not require re-description of what was already known. *Capon v. Dudas*, 418 F.3d 1349, 1357 (Fed Cir 2005). Thus, the present application's claim of priority to the '665 application extends to the subject matter of claims 51-55. Applicants request recognition of priority to U.S. Provisional patent application serial number 60/137,665, filed on June 4, 1999, for claims 51-55. Therefore, claims 51-55 are entitled to the priority date of June 4, 1999.

IV. Rejections under 35 U.S.C. § 112, second paragraph

The Action rejects claims 19-21, 27-33, and 51-56 as indefinite under 35 U.S.C. §112, second paragraph based on the use of the relative term "derived." Applicants have amended the claims to remove the unnecessary phrase "GBV-B derived" from the claim preamble. This amendment to the preamble clarifies, but does not alter the claimed invention. The rejection based on the phrase "derived" is moot.

V. Rejections under 35 U.S.C. § 112, first paragraph

The Action rejects claims 19-20, 27-33, and 51-56 as lacking enablement under 35 U.S.C. §112, first paragraph based on the alleged lack of enabling disclosure for the inventive methods. The Action alleges that the broad scope of the claims read on any recombinant virus

genome and any type of host cell. Furthermore, the Action takes the position that the art was unpredictable. The Action's position is that these factors result in the non-enablement of the present invention. The Applicants respectfully traverse.

First, the Action improperly interprets the present claims. The present claims are not directed to methods of producing any virus in any host cell. Amended claim 19 reads "introducing into a host cell a recombinant *GBV-B or chimeric GBV-B viral genome*." (emphasis added) Also, the claims are directed to a cell cultured under conditions that permit production of a virus from the viral genome. The Action misreads the plain text of the present claims to include any virus (including fragments) and any host cell.

Furthermore, one of skill in the art knows how to introduce a viral genome into a host cell and how to determine if a cell was permissive for virus production (De Tomassi *et al.*, 2002(Exhibit B) and Yi *et al.*, 2005 (Exhibit C)). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). One of skill would have been able to identify a cell permissive for virus production based on the present disclosure. For example, Yi *et al.* (one skill in the art) describe the production of a HCV infection in cell lines transfected with genotype 1a HCV, which is closely related to the GBV-B virus. (see abastract Yi *et al.*, 2005). One of skill would recognize that similar methodology can be used for the identification of a cell permissive GBV-B virus.

The Action attempts to rebut this position by citing the Buckwold *et al.* reference. The Action takes the position that Buckwold *et al.* provides a sufficient description of the methodology claimed to render the art unpredictable. The methodology used by Buckwold *et al.* is not disclosed in the publication and cannot be scrutinized for scientific rigor or used for

comparison with published methods that have resulted in identification of a permissive cell line. In fact, Buckwold *et al.* contradicts the results presented in De Tomassi *et al.* (2002) (Exhibit B). De Tomassi states "[] *in vitro* transcribed RNA was used to transfect the Huh7 human hepatoma cell line, and intracellular replication of transfected RNA was shown to occur..."(see abstract). This gives Applicants concern that the results of Buckwold *et al.* are unsound and insufficient to establish unpredictability in the art, or in the least contradict previous publications. The Action elevates the results of one suspect publication to be dispositive in determining the enablement of the present claims.

Applicants have added claims 57-72 to further clarify certain aspects of the invention related to the presently claimed subject matter. The new claims are directed to using a genome comprising a 3' sequence with a stated percent identity to SEQ ID NO:1, using liver cells, and using viral replication as an endpoint. Applicants do not disclaim the scope of the previously presented claims and add these claims to further cover various aspects of the invention. Applicants respectfully request the additional examination of new claims 57-72.

VI. Rejections under 35 USC § 102

The Action rejects claims (A) 19-20, 28-33, 51-54, and 56 as anticipated under 102(e) by U.S. Patent 6,627,437 ('437 patent) in light of Sbardellati *et al.* (2001); and (B) 51-54 as anticipated under 102(a) by Bukh *et al.* (1999). Applicants respectfully traverse.

A. Claims 19-20, 28-33, 51-54 and 56 are Patentable over Traboni and Sbardellati *et al.*

Claims 19-20, 28-33, 51-54 and 56 are rejected as being anticipated by '437 patent in light of Sbardellati *et al.* (2001). Applicants traverse.

Neither the '437 patent or the Sbardellati reference are prior art under 35 U.S.C. §102(e). As stated in the Action 35 U.S.C. §102(e) at the time of filing reads:

> A person shall be entitled to a patent unless [] (e) the invention was described in a patent granted on an application for patent by another *filed in the United States* before the invention thereof by the application for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent. (emphasis added)

The '437 patent was filed in the United States on May 25, 2000. The effective filing date of a reference under 35 U.S.C. §102(e) is the United States filing date, not the foreign application priority date. (MPEP §2136.03; *In re Hilmer*, 359 F.2d 859, 883(CCPA 1966)). The effective filing date under 35 U.S.C. §102(e) for the '437 patent is May 25, 2000. Applicants' priority date is June 4, 1999. Therefore, on its face the '437 patent is not 102(e) prior art. Further, the description provided in the Sbardellati reference is irrelevant to the sufficiency of the '437 patent as either a prior art reference under 102(e) or as anticipating the present invention. It is not prior art. Applicants request withdrawal of the rejection.

B. Claims 51-54 are patentable over Bukh *et al.*

Claims 51-54 as rejected as anticipated under 102(a) by Bukh *et al.* (1999). Applicants traverse.

Claims 51-54 are entitled to the priority date of June 4, 1999, as described above and incorporated here by reference. Therefore, the Bukh *et al.* reference published in September of 1999 is not a description of the invention in a printed publication in this country before the invention of claims 51-54. Applicants request withdrawal of the rejection.

CONCLUSION

Applicants believe that the present document is a full and complete response to the Action dated November 28, 2005. The present case is in condition for allowance, and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned Agent at (512) 536-3167 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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